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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,731	05/11/2001	Apollon Papadimitriou	20619	6504

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PATENT LAW DEPARTMENT
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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,731	PAPADIMITRIOU, APOLLON	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-17,19,23-36,38-42,44,48-55,59-61,67-77 and 83-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13-17,19,23-36,38-42,44,48-55,59-61,67-77 and 83-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/13/04;9/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the previous Office Action dated May 12, 2004 is withdrawn due to a new ground rejection.

Status of the Claims

2. Claims 1-11, 13-17, 19, 23-36, 38-42, 44, 48-55, 59-61, 67-77 and 83-89 are pending.

Applicants' amendment filed on June 7, 2004 is acknowledged. Applicants' response has been fully considered. Claims 13, 38, 71, 73, 75 and 76 have been amended. Thus, claims 1-11, 13-17, 19, 23-36, 38-42, 44, 48-55, 59-61, 67-77 and 83-89 are examined.

Objection Withdrawn

3. The previous objection of claims 71, 73 and 75 is withdrawn in view of applicant's amendment to the claims, and applicant's response at page 19 of the amendment filed June 7, 2004.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 13-17, 38 and 76 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in view of applicant's amendment to the claims, and applicant's response at page 19 of the amendment filed June 7, 2004.

Claim Objections

4. Claims 1, 3, 26, 28, 51, 67, 69, 71, 73 and 75 are objected to because of the use of the term "multipli-charged" or "multiply charged". Please use the term with correcting spelling.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 19, 26, 44 and 67-76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/014,363 (corrected from previous 10/041,363). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 19, 26, 44 and 67-76 in the instant application disclose a liquid pharmaceutical composition comprising an EPO glycoprotein product having the in vivo biological activity, wherein the glycoprotein product is a pegylated EPO such as EPO being linked to $-CO-(CH_2)_x-(OCH_2CH_2)_m-OR$. This is an obvious variation in view of claims 1-16 in the copending application which disclose a conjugate comprising an EPO glycoprotein having N-terminal α-amino group and one poly(ethyleneglycol), where EPO is linked to $-CO-(CH_2)_x-(OCH_2CH_2)_m-OR$, and a pharmaceutical composition comprising the conjugate. Both the claims of the instant application and the claims of the copending application are directed to a pharmaceutical composition comprising a conjugate of EPO with poly(ethyleneglycol). Claims 1, 19, 26, 44 and 67-76 in present application and claims 1-16 in the copending application are obvious variations of a pharmaceutical composition comprising a conjugate of EPO with poly(ethyleneglycol) having the in vivo biological activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In response, applicants cite the same reason as previously indicated (see pages 18-19 of the response filed February 17, 2004). The ground of rejection remains until all other issues resolved.

6. Claims 1-11, 13-17, 19, 23-36, 38-42, 44, 48-55, 59-61, 67-77 and 83-89 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of copending Application No. 10/780,297 (US 2004/0147431). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-11, 13-17, 19, 23-36, 38-42, 44, 48-55, 59-61, 67-77 and 83-89 in the instant application disclose a liquid pharmaceutical composition comprising an EPO glycoprotein product having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and the liquid composition comprises a therapeutically effective amount of EPO product and is stable at room temperature for at least 6 months and not containing urea. This is an obvious variation in view of claims 1-59 in the copending application which disclose a liquid pharmaceutical composition consisting essentially of an EPO glycoprotein product having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and the liquid composition comprises a therapeutically effective amount of EPO product. Both the claims of the instant application and the claims of the copending application are directed to a pharmaceutical composition comprising an EPO glycoprotein product, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0. Claims 1-11, 13-17, 19, 23-36, 38-42, 44, 48-55, 59-61, 67-77 and 83-89 in present application

and claims 1-59 in the copending application are obvious variations of a pharmaceutical composition comprising an EPO glycoprotein product having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and the liquid composition comprises a therapeutically effective amount of EPO product.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 4-5, 9-10, 14-17 and 29-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 4-5 and 29-33 are indefinite because the claim cites citrate being a multiple charged inorganic anion, in fact citrate is an organic acid. Claims 5 and 30-33 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

9. Claims 9-10 and 34-35 are indefinite as to arginine/H_2SO_4/Na_2SO_4 being a buffer for pH 5.5-7.0 because argnine has a pKa of 1.8, 9 and 12.5, and H_2SO_4 is a strong acid, it is not clear how the combination can be used as a buffer. Claims 10 and 35 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

10. Claim 14 recites the limitation "the amino acid sequence of the erythropoietin is modified" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim because claim 13 only indicates the EPO sequence, it does not indicate the modification of the sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4, 6-9 and 11 are rejected under 35 U.S.C. 102(b) as anticipated by Yamazaki *et al.* (EP 0909564, April 25, 1997).

Yamazaki *et al.* disclose a solution preparation of EPO containing biologically active EPO including human EPO; an amino acid such as lysine, arginine or histidine as a stabilizer; polyethylene glycol; sugars; inorganic salt such as sodium chloride; and phosphate and/or citrate as a buffer with a pH of 5.0 to 8.0 (page 3; claims 1-4, 6-9 and 11). With the addition of histidine, the EPO is stable for 6 months at 25 °C (Table 5).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-4, 6-9, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamazaki *et al.* (EP 0909564) in view of Rosen *et al.* (WO 92/06116).

Yamazaki *et al.* disclose a solution preparation of EPO containing biologically active EPO including human EPO; an amino acid such as lysine, arginine or histidine as a stabilizer; polyethylene glycol; sugars; inorganic salt such as sodium chloride; and phosphate and/or citrate as a buffer with a pH of 5.0 to 8.0 (page 3; claims 1-4, 6-9 and 11). However, Yamazaki *et al.* do not disclose the amino acid sequence of human EPO. Rosen *et al.* teach the amino acid sequence of recombinant human EPO (page 7, lines 32-34; SEQ ID NO:3 of WO 92/06116). At the time of invention was made, it would have been obvious that one of ordinary skill in the art is motivated to use the recombinant human EPO taught by Rosen *et al.* to prepare the pharmaceutical composition as taught by Yamazaki *et al.* (claim 13) because the use of recombinant protein would avoid the possibility of contamination from tissue. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

13. Claims 1-4, 6-9, 11 and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamazaki *et al.* (EP 0909564) in view of Rosen *et al.* (WO 92/06116) as applied to claims 1-4, 6-9, 11 and 13 above, further in view of in view of Elliot *et al.* (EP 0640619).

The combination of Yamazaki *et al.* and Rosen *et al.* disclose a solution preparation of EPO containing biologically active EPO including human EPO or erythropoietin having the amino acid sequence of SEQ ID NO:1 or 2; an amino acid such as lysine, arginine or histidine as a stabilizer; polyethylene glycol; sugars; inorganic salt such as sodium chloride; and phosphate and/or citrate as a buffer with a pH of 5.0 to 8.0 (page 3; claims 1-4, 6-9, 11 and 13). However,

Yamazaki *et al.* and Rosen *et al.* do not disclose the use of a modified human EPO in the composition. Elliot *et al.* teach EPO analogs having at least one additional site for glycosylation or a rearrangement of at least one site for glycosylation, such as the modified EPO with $Asn^{30}Thr^{32}Val^{87}Asn^{88}Thr^{90}$ (page 3, lines 21-28; page 19, Table 3, line 22). At the time of invention was made, it would have been obvious that one of ordinary skill in the art is motivated to use the modified human EPO taught by Elliot *et al.* to prepare the pharmaceutical composition as taught by Yamazaki *et al.* and Rosen *et al.* (claims 14-17) because the modified EPO having additional glycosylation site would have better in vivo activity due to its higher sialic acid content in the glycosylated protein. Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
October 1, 2004

JON WEBER
SUPERVISORY PATENT EXAMINER